REMARKS

Claims 1-8, 10-17 and 22-25 are currently pending in the application.

Claims 8-15 and 18-21 have been canceled. Claims 1, 4, 16, 17, 22 and 24 have been amended. No new matter has been added by these amendments.

Applicants thank the Examiner for removing several of the objections and rejections from the last office action.

Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 8 and 10-17 have been rejected under 35 U.S.C. § 112, second paragraph, because the claims allegedly do not recite a contact step for the detection of a natriuretic peptide in the bodily fluid sample. Claims 8 and 10-15 have been canceled, thus rendering the rejection moot. Claims 16 and 17 are now dependent from claim 1, which recites a contacting step, and therefore the rejection is moot in regard to claims 16 and 17. Accordingly, Applicants request the reconsideration and withdrawal of the rejections for indefiniteness.

Claim Rejections – 35 U.S.C. § 112, first paragraph - enablement

Claims 1-8 and 10-17 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, because the specification is allegedly not enabling for embodiments wherein an antibody is specific for an immunoreactive fragment of the ORP150 comprising SEQ ID NO: 2. Applicants have amended claim 1 to remove the phrase "an immunoreactive fragment."

Claims 1-8 and 10-17 have been further rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, because the specification is allegedly not enabling for the term "in the format of." Applicants have amended claim 4 to remove the phrase "in the format of" and simply recite "an immunoassay." Support for embodiments wherein the claimed method is performed as an immunoassay is present throughout the specification.

Finally, claims 1-8 and 10-17 have been further rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, because the specification is allegedly not enabling for "any" "natriuretic polypeptide," "N-BNP" or "BNP" without reference to a specific polypeptide sequence for the recited "natriuretic polypeptide,"

"N-BNP," or "BNP." Applicants have amended claim 1 to recite "brain natriuretic peptide (BNP) or N-terminal pro-brain natriuretic peptide (N-BNP)" rather than simply "natriuretic polypeptide." What is encompassed by the terms "BNP" and "N-BNP," and how to make and use BNP and N-BNP, is supported throughout the specification, both verbatim and by incorporating by reference articles describing BNP and N-BNP (see, e.g., page 1, page 6, pages 9-10, etc.) A sequence of BNP or N-BNP is not necessary for one of skill in the art to be able to detect BNP or N-BNP in a sample; methods for doing so and reagents for doing so are well-known and widely available in the art. N-BNP is derived from the precursor of BNP and is considered a reasonable alternative to using BNP in diagnosing conditions such as LVSD. Thus, although the working examples in the specification illustrate the successful use of N-BNP in conjunction with ORP150, it would not constitute undue experimentation for one of skill in the art to adapt the assays for use with BNP instead.

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for lack of enablement.

Claim Rejections – 35 U.S.C. § 112, first paragraph - written description

Claims 1-8 and 10-17 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Specifically, it is alleged that there is no written description for embodiments wherein an antibody is specific for an immunoreactive fragment of the ORP150 comprising SEQ ID NO: 2, for the term "in the format of," and for the terms "natriuretic polypeptide," "N-BNP," or "BNP."

As described above, Applicants have amended claims 1 and 4 to render the rejection moot as it relates to the terms "immunoreactive fragment" and "in the format of."

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. As argued above, Applicants have clearly described in the specification what is meant by "N-BNP" and "BNP" in detail and by incorporation by reference. A sequence of BNP or N-BNP is not necessary for one of skill in the art to be able to detect BNP or N-BNP in a sample; methods for doing so and reagents for doing so are well-known and widely available in the art. Most references describing an assay for detection of BNP or N-BNP do not provide the sequence of either molecule, yet there is no doubt

the authors had possession of the disclosed assay. Applicants have reduced to practice at least one assay for N-BNP, and have described other species in the genus of what is BNP and N-BNP in sufficient detail such that one of skill in the art would know what was meant by the terms.

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for lack of written description.

Claim Rejections – 35 U.S.C. § 103

Claims 1-4, 7-8, 10-11 and 14-17 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al.

The '637 patent does not teach or suggest a method for detecting tissue hypoxia in a mammalian subject by contacting a bodily fluid sample with an antibody specific for an oxygen related protein 150 (ORP150) comprising SEQ ID NO: 2 or an immunoreactive fragment thereof in order to detect the level of ORP150 in the bodily fluid sample, whereby an elevated level of ORP150 relative to normal is indicative of an increased risk of heart disease. Hall is relied on by the Examiner as teaching the detection of natriuretic peptide, particularly in combination with other diagnostic tests.

Applicants respectfully assert that the Examiner has misconstrued the teachings of Hall. Hall discusses in section 7 whether the natriuretic peptide measurements would make other diagnostic examinations superfluous and discusses whether the natriuretic peptide measurements could replace the existing gold standard or only be used to supplement current methods. Thus, it does not teach or suggest the desirability of combining the natriuretic peptide measurements with *any* other diagnostic that might be developed later on, nor does it teach or suggest the mode, e.g. using a computer program (logistic regression analysis), by which the two measurements could be combined. Further, it is not obvious why measurement of a protein increased by hypoxia combined with another protein increased in heart failure would provide for an improvement in accuracy of the diagnostic; such a combination would not have afforded predictable results. Hall does not provide any insight into this issue. Applicants respectfully submit that based on the teachings of Hall, one of skill in the art would not have been motivated to combine a completely novel diagnostic based on another protein as taught in the '637 patent.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al.

Claims 4-5 and 11-12 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of Karl et al.

As discussed above, the combination of the '637 patent with Hall does not render claims 1-4, 7-11 and 14-17 obvious. The addition of Karl et al does not remedy this deficiency.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of Karl et al.

Claims 4, 6, 11 and 13 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of May et al.

As discussed above, the combination of the '637 patent with Hall does not render claims 1-4, 7-11 and 14-17 obvious. The addition of May et al does not remedy this deficiency.

Thus, Applicants respectfully request reconsideration and withdrawal of the rejection for obviousness over U.S. Patent No. 5,948,637 in view of Hall et al. and further in view of May et al.

Claim Rejections – 35 U.S.C. § 112, first paragraph - new matter

Claims 1-8 and 10-17 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter in the form of the terms "an immunoreactive fragment thereof" and "in the form of". Claims 1 and 4 have been amended to remove these terms, thus rendering the rejection moot.

Accordingly, Applicants request the reconsideration and withdrawal of the rejections for presence of new matter.

CONCLUSION

Early and favorable consideration of the application is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000.

Respectfully submitted,
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